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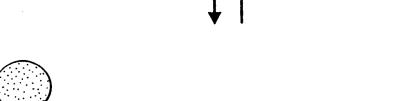
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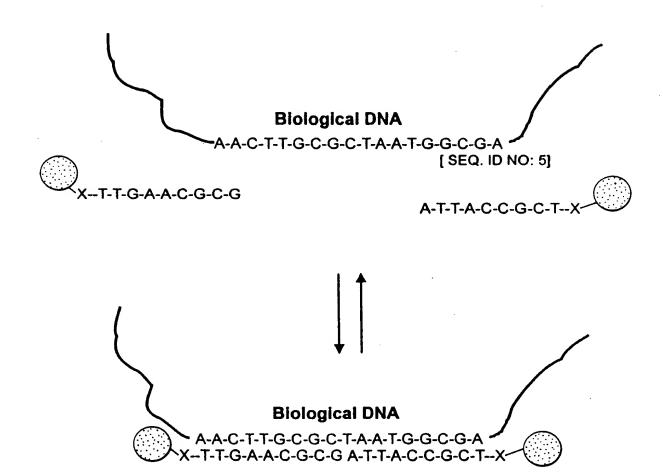
[SEQ. ID NO: 3] X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C 5'

G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X
3' [SEQ. ID NO: 4]

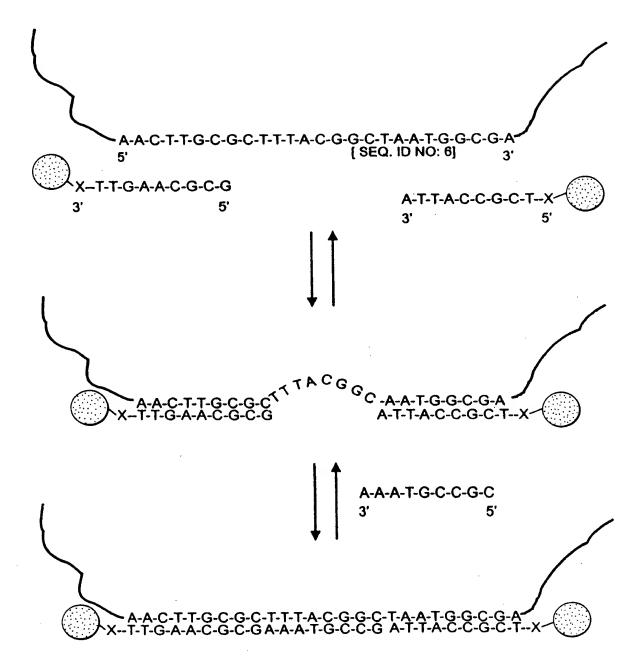


(-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X[~]











Linking oligonucleotide FIG. 4 A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G A-T-A-T-G-C-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A 3' A-T-A-T-G-C-G-C-G-A-T-C-T-C-T-C-A-G-C-A-A-A 5' [SEQ. ID NO: 2]

[SEQ. ID NO:1]

Colloids

Mix below Tm Heat 3' 5' A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G A-G-T-C-G-T-T-T-T--> X-T-A-C-C-G-T-T-G A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A 3' 5'

Aggregate-

Stand below Tm

Heat

Precipitate (formed by further cross-linking)



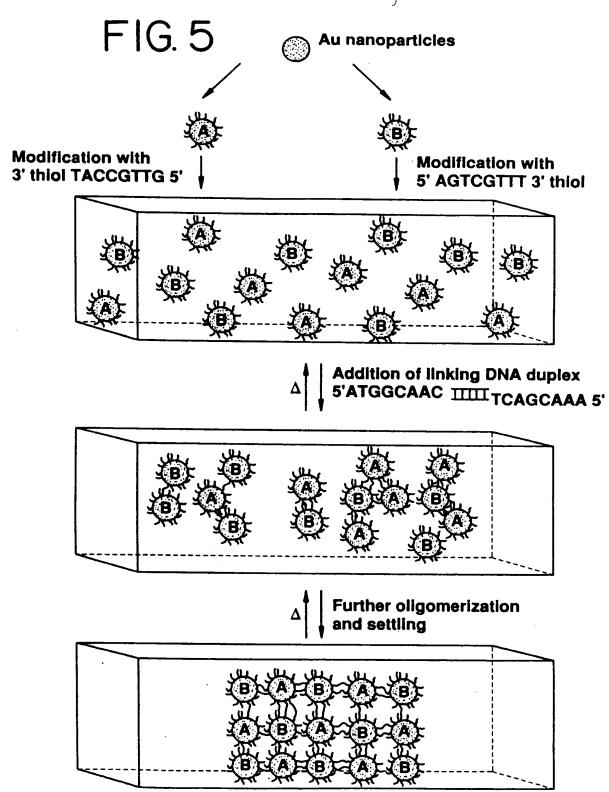
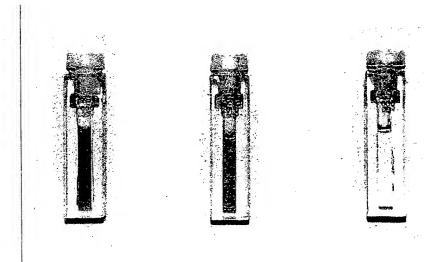
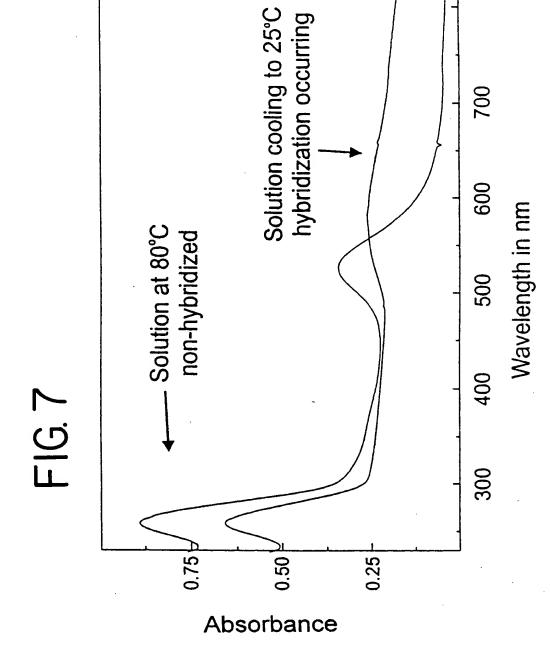




FIG. 6A FIG. 6B FIG. 6C









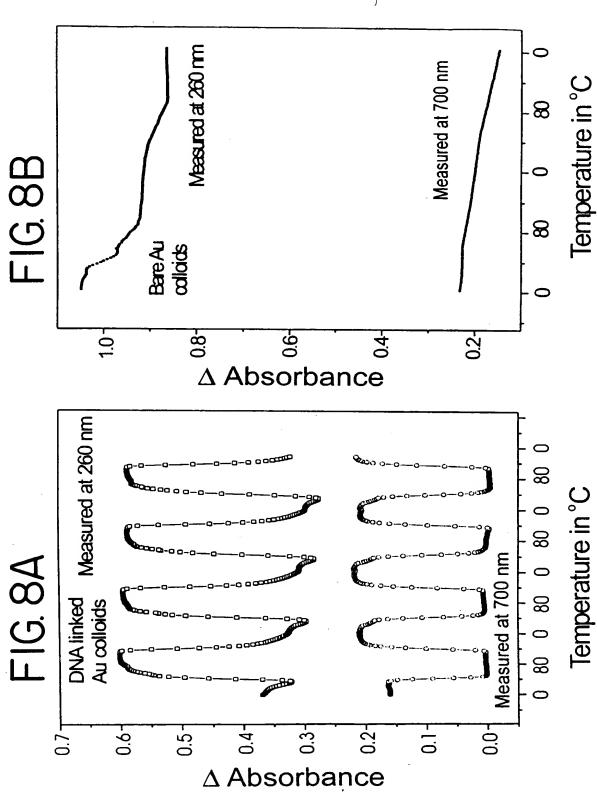




FIG. 9A

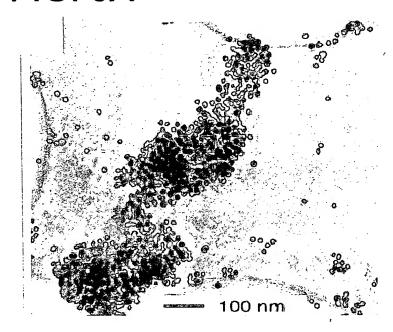
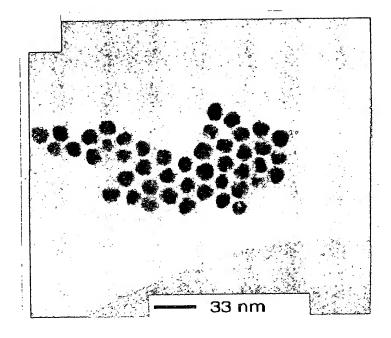


FIG. 9B



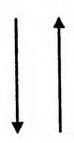


[SEQ ID NO: 7]

5'
3'
X--T-C-T-C-C-C-T-T-T-C
A-G-A-G-G-A-A-G-G-X
3'

[SEQ ID NO: 8]

3' T-C-T-C-C-T-T-C-C-C-T-T-T-T-C 5' [SEQ ID NO: 9]



5' 3' X--T-C-T-C-C-T-T-C-C-C-T-T-T-C A-G-A-G-G-A-A-G-G-A-A-A-A-G-X 3' T-C-T-C-C-T-T-C-C-C-T-T-T-T-C 5'



F1G. 1

's-A-T-G-G-C-A-A-C-T-A-C-G-C-G-C-T-A-G-A-G-T-C-G-T-T-T _[SEQ. ID NO: 10]

SEO. I

.



FIG. 12A 12/47 Complementary Target [SEQ. ID NO: 14] [SEQ. ID NO:12] 5' A-G-C-A-T-G-G-T-C-G-A-T-A-G-G-A-A-A-C-G-A-C-T-C-T-A-G-C-G-C SEQ. ID NO:13 FIG. 121 **Probes without Target** T-T-T-G-C-T-G-A-G-A-T-C-G-C-G 3' T-C-G-T-A-C-C-A-G-C-T-A-T-C-C FIG. 12C **Half Complementary Target** [SEQ. ID NO: 15] FIG. 12D Target - 6 bp 5' G-T-C-G-A-T-A-G-G-A-A-A-C-G-A-C-T-C-T-A-G-C-G-C [SEQ. ID NO: 16] FIG. 12E One bp Mismatch 3' T-C-G-T-A-C-C-A-G-C-T-A-T-C-C T-T-T-G-C-T-G-A-G-A-T-C-G-C-G 5' A-G-C-A-T-G-G-T-T-G-A-T-A-G-C-A-A-A-C-G-A-C-T-C-T-A-G-C-G-C [SEQ. ID NO: 17] FIG. 12F Two bp Mismatch 3' T-C-G-T-A-C-C-A-G-C-T-A-T-C-C T-T-T-G-C-T-G-A-G-A-T-C-G-C-G 5' A-G-C-A-T-G[T]T[T]G-A-T-A-G-G-A-A-A-C-G-A-C-T-C-T-A-G-C-G-C SEQ. ID NO: 18]





FIG. 13A

transparent substrate

Modified DNA chemisorbed onto solid substrate

} A'

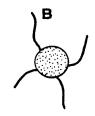
Analyte DNA

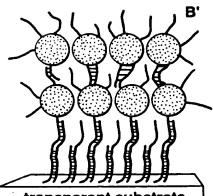
B'

transparent substrate

Analyte DNA hybridized onto substrate

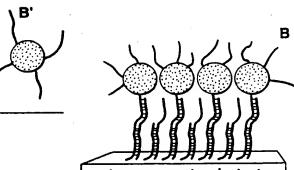
DNA modified colloids





transparent substrate

Dark areas where nanoparticle aggregates are linked to substrate surface by analyte DNA



transparent substrate

DNA modified colloids hybridized to bound analyte DNA

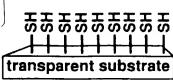


FIG. 13B

14/47

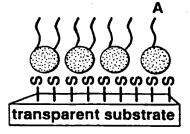
transparent substrate

thiol terminated modification of surface



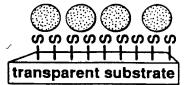
gold nanoparticles

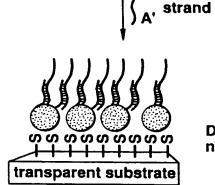




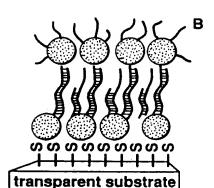
thiol modified DNA adsorbed onto particles

analyte DNA





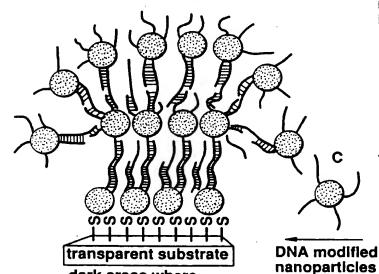
DNA modified nanoparticles



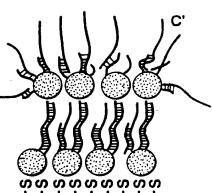
analyte DNA hybridized to DNA modified nanoparticles







dark areas where
nanoparticle aggregates linked
to substrate by analyte DNA



transparent substrate





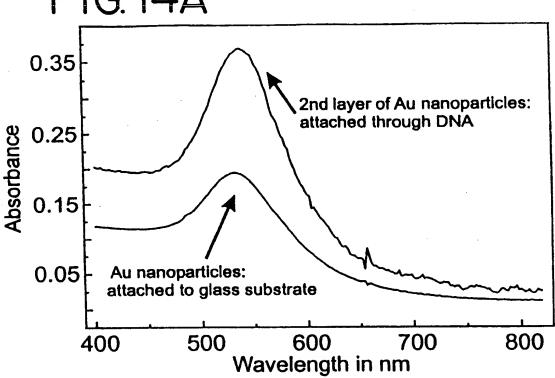
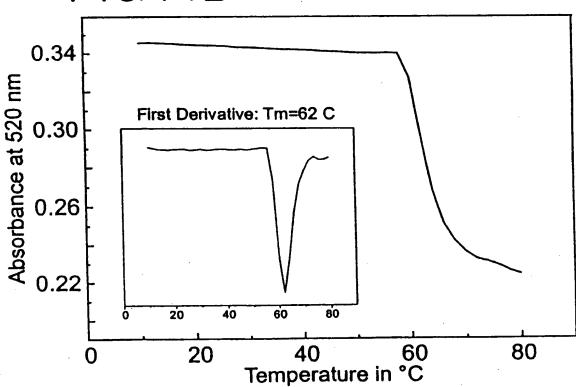
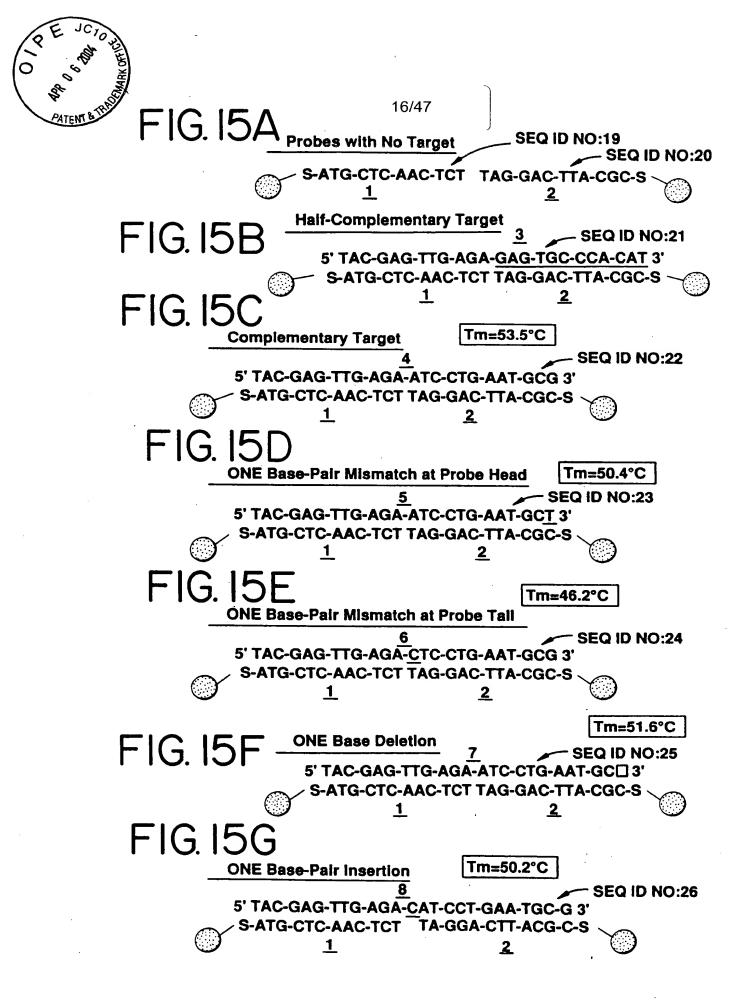
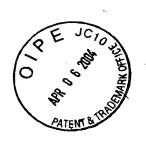


FIG. 14B







F1G. 16A

24 Base Template

- S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S 5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'

FIG. 16B

48 Base Template with Complementary 24 Base Filler

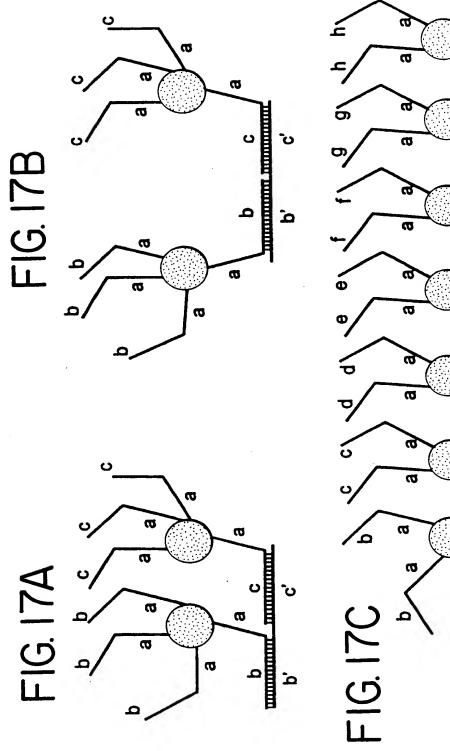
5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3' >> S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S

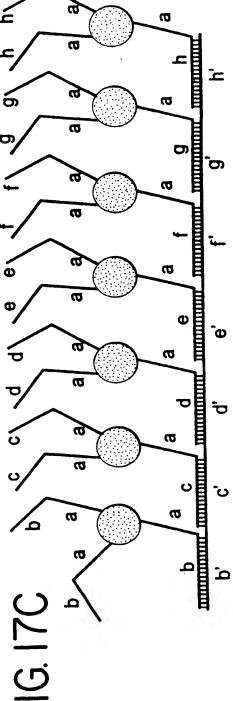
FIG. 16C

72 Base Template with Complementary 48 Base Filler

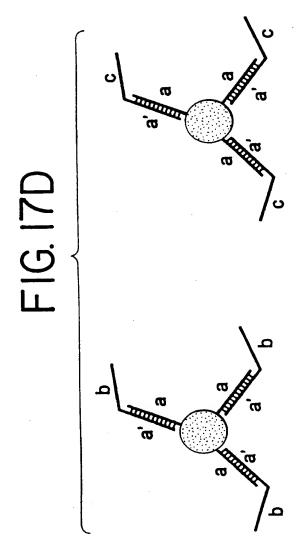
✓ S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT-ATA-TAA-CCT-GCG-AAA-TGC-CTG-TTG TAG-GAC-TTA-CGC-S ~ 5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-TAT-ATT-GGA-CGC-TTT-ACG-GAC-AAC-ATC-CTG-AAT-GCG 3'

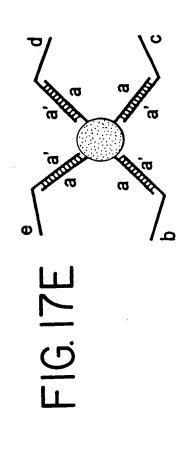














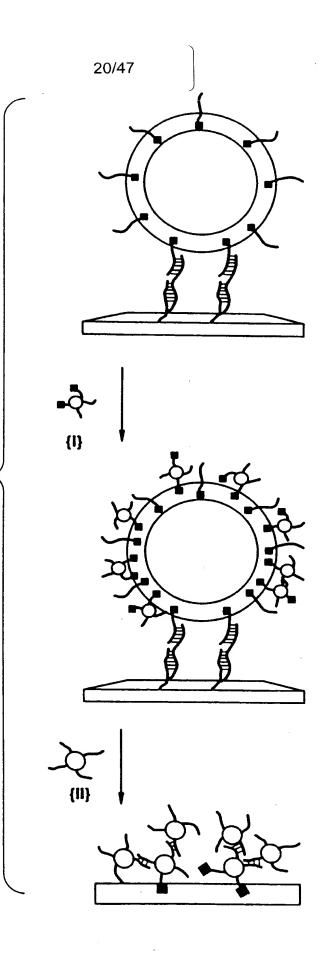




FIG. 19A

21/47

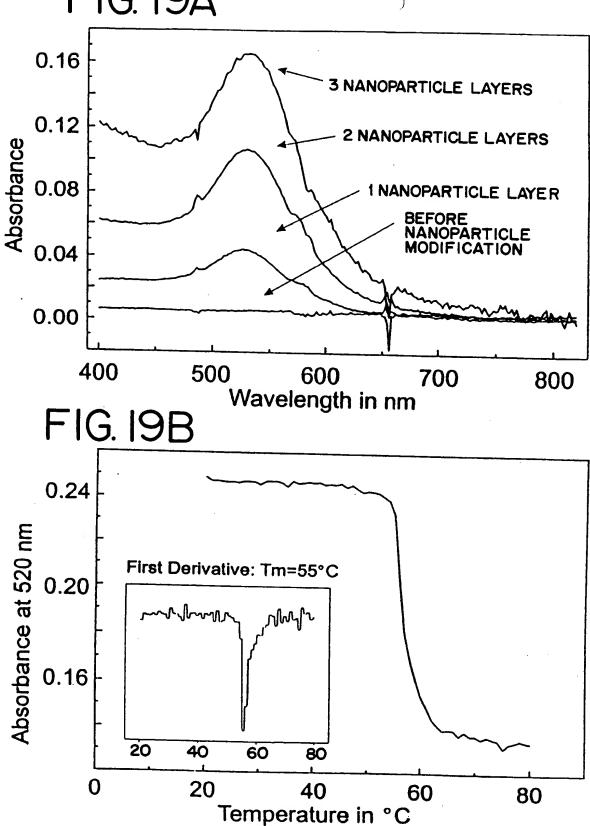
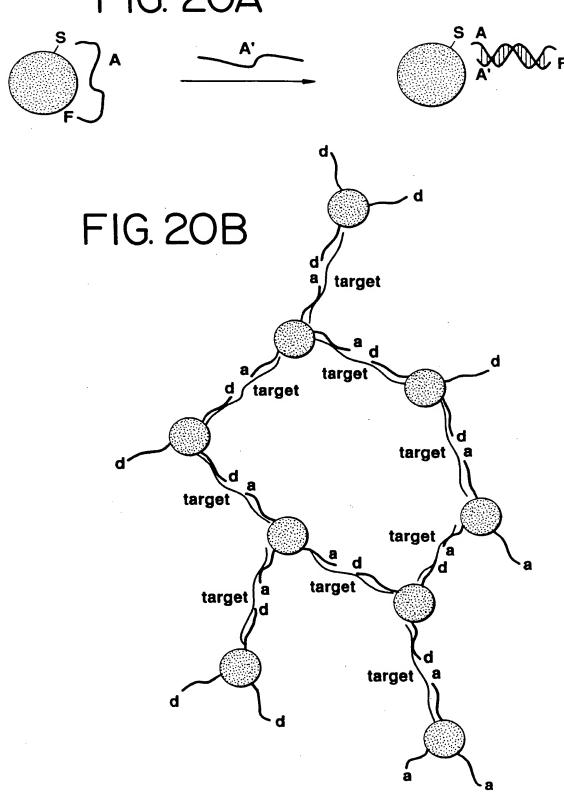




FIG. 20A

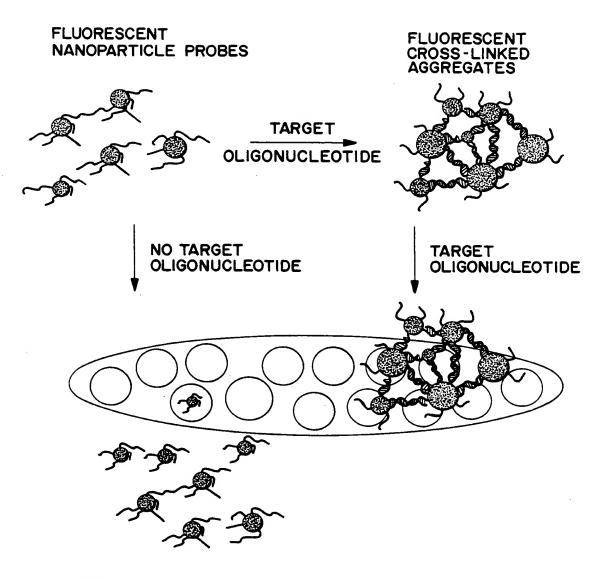


membrane



Pink/Non-fluorescent Excess Au probes Au/Latex hybrid pass through Target Oligonucleotide 0000 Oligonucleotide Target oligonucleotide modified Fluorophore labeled White/Fluorescent Oligonucleotide 0 latex probes No Target nanoparticle probes 0000 All Au probes pass through membrane Oligonucleotide modified Au Red F16.21





THE FLUORESCENT NANOPARTICLE PROBES PASS THROUGH THE MEMBRANE

THE FLUORESCENT CROSS-LINKED AGGREGATES ARE RETAINED BY THE MEMBRANE



Anthrax PCR Product

5'G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT 3'C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA <u>GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT</u> ATA AGA AAA AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3' TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

141 mer Anthrax PCR product [SEQ ID NO:36]

3' CTC CCT AAT AAC AAT

3' TTA TAA CTA TTC CTA -

[SEQ ID NO:38] ·

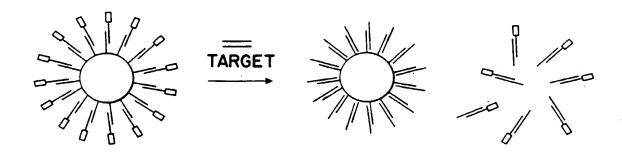
Oligonucleotide-Nanoparticle Probes

Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT	[SEQ ID NO:39]
3' A TCT CTT CAT TAA TTA AGC AGT TGT	[SEQ ID NO:40]
3' TAT TCT TTT TAT AAT AGG TCC CAA TAT	[SEQ ID NO:41]
3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA	[SEQ ID NO:42]

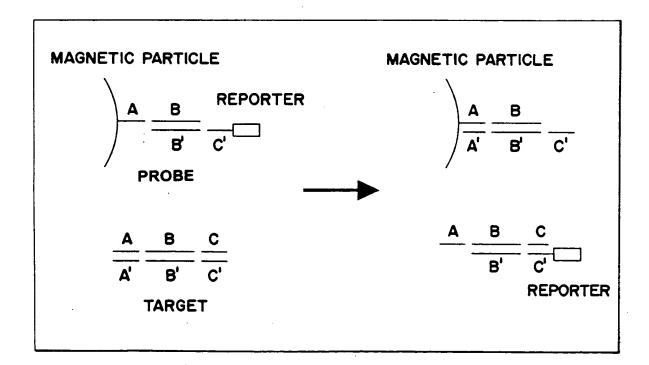






SATELLITE PROBE

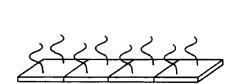
DETECTION SIGNAL





27/47

FIG. 25A





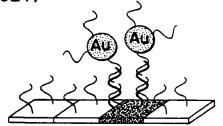
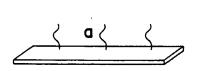
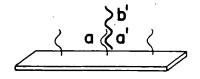
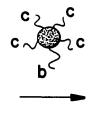


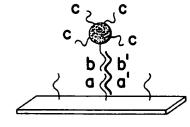
FIG. 25B

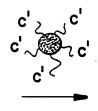


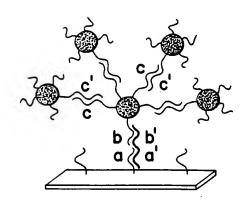












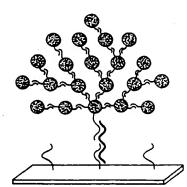




FIG. 26A

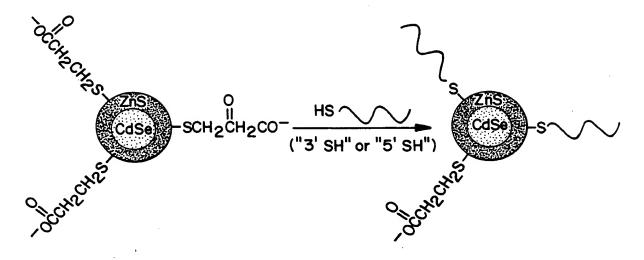
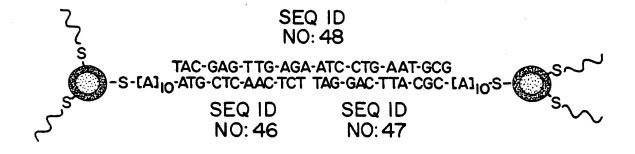


FIG. 26B





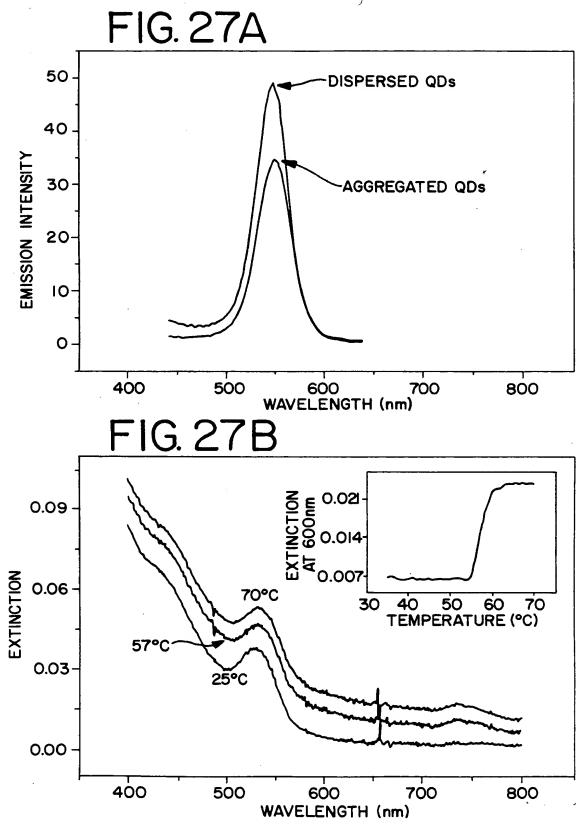




FIG. 27C

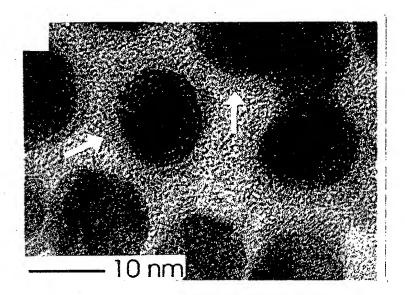


FIG. 27D

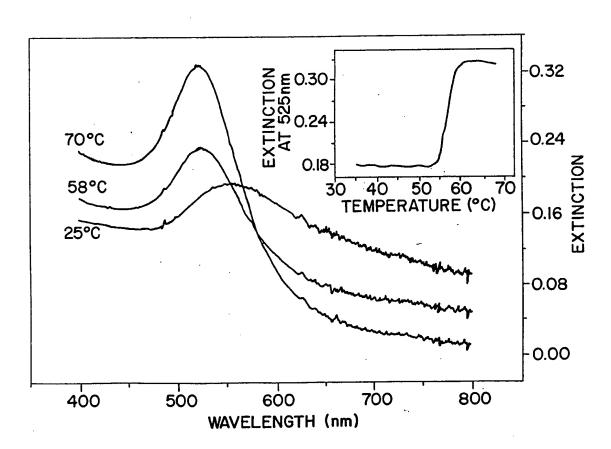




FIG. 28A





FIG. 28B

FIG. 28C

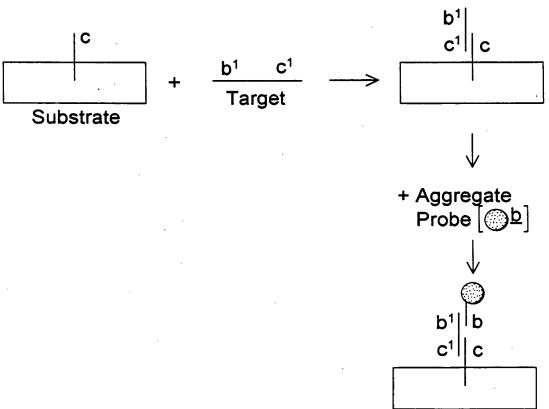




FIG. 28D

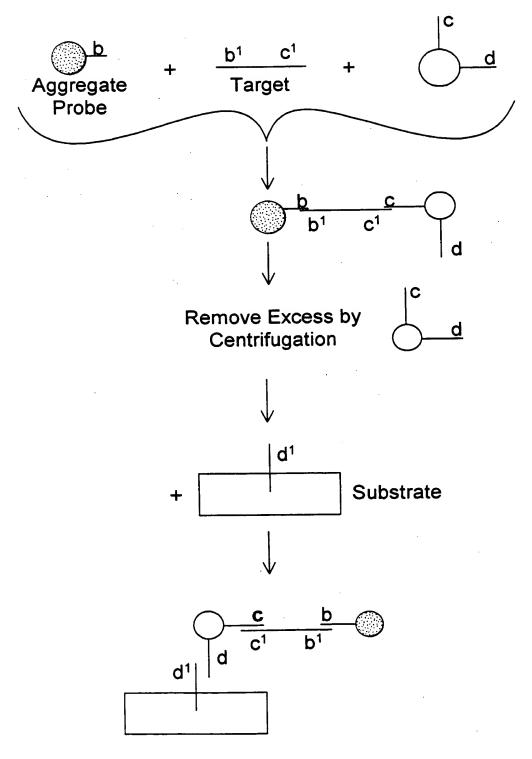
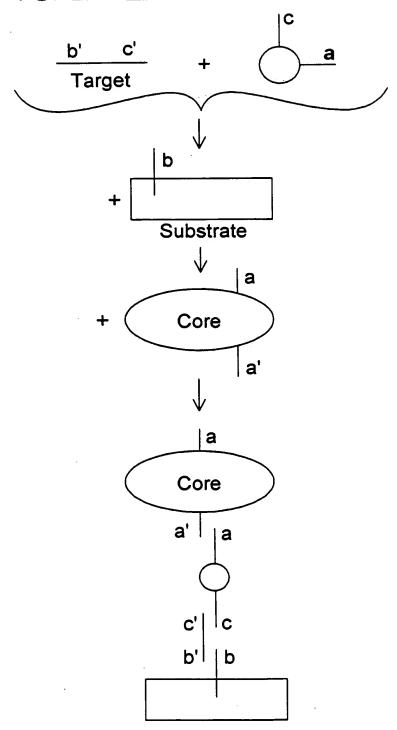
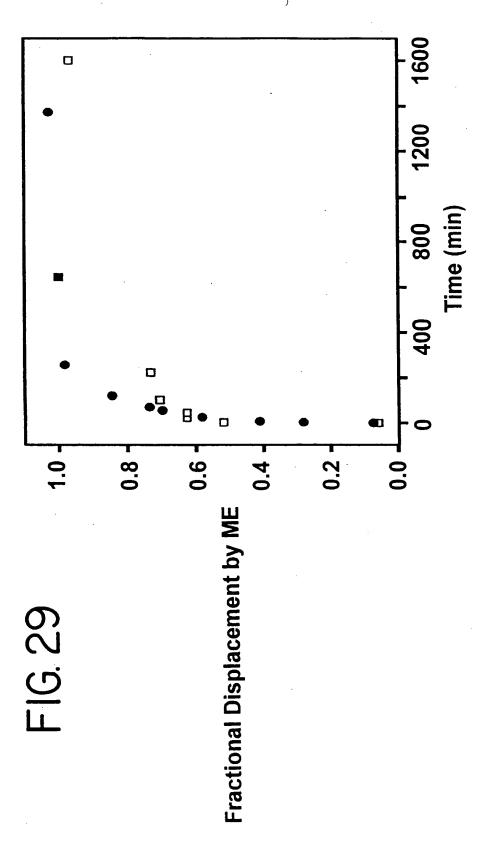


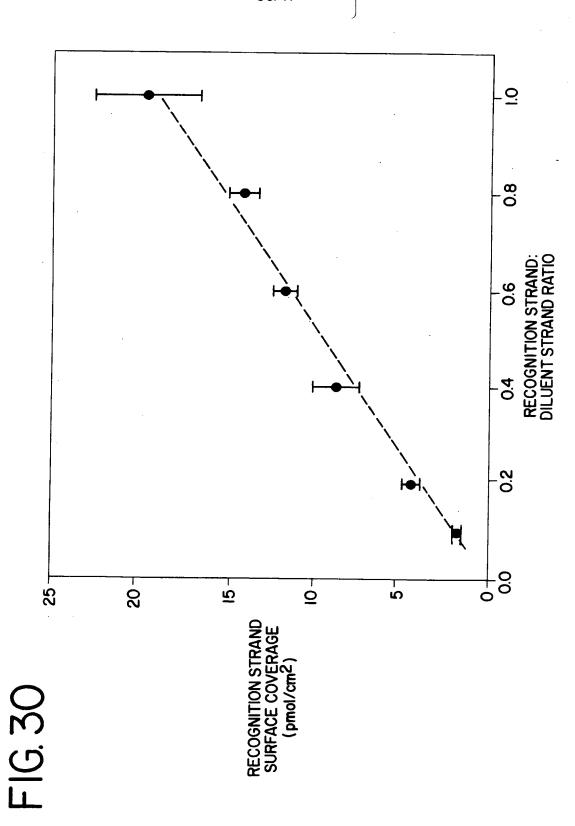


FIG. 28E











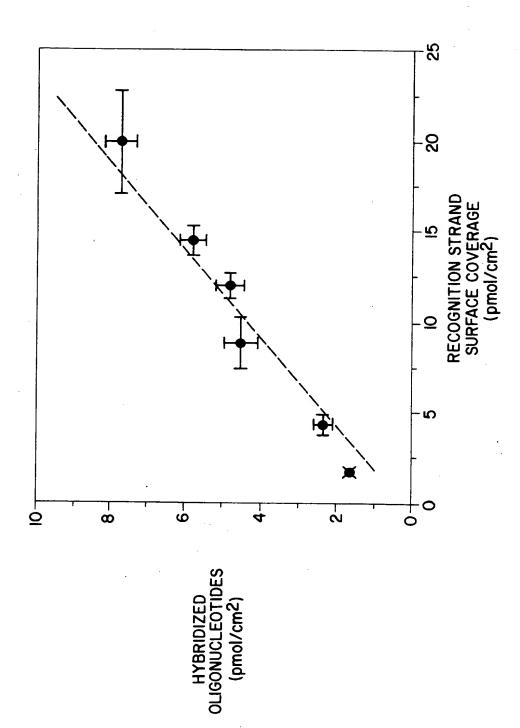




FIG. 32

[SEQIDNO:56]

5' GGA T**T**A TTG TTA- -AAT ATT GAT AAG GAT 3' CCT A**N**T AAC AAT TTA TAA CTA TTC CTA \(\simeq \)

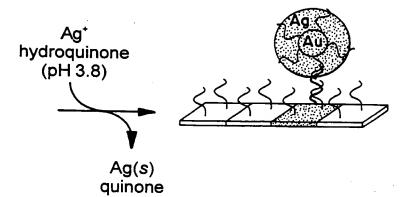
[SEQ ID NO: 57]

[SEQ ID NO: 58]

N = A (complementary), G,C,T (mismatched)

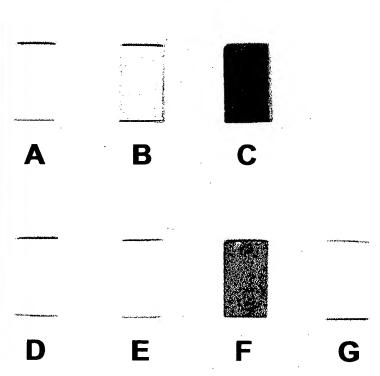
1. \to (target DNA)

2.

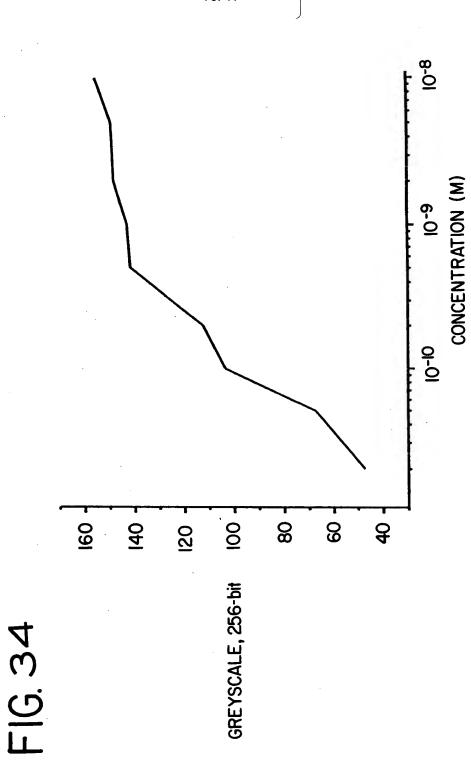






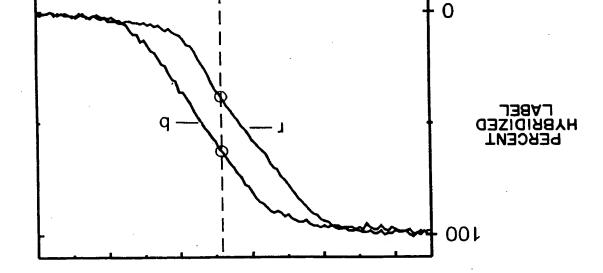












SO

OI

FIG.35A

30 40 (°C)

09

09

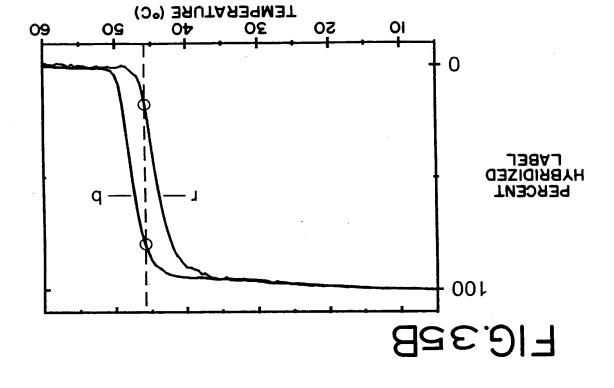






FIG. 36A

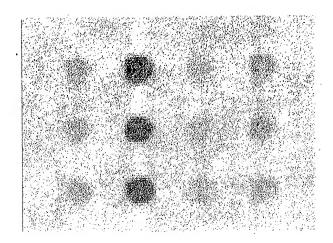
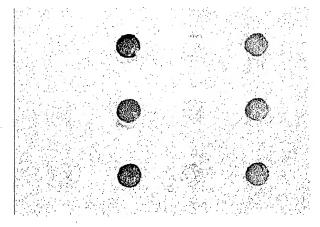


FIG. 36B



CATG



FIG.37A

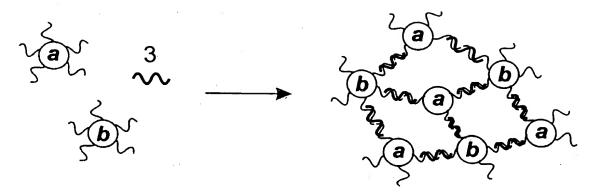
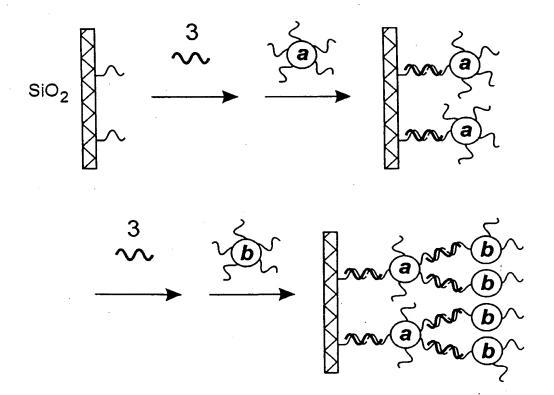
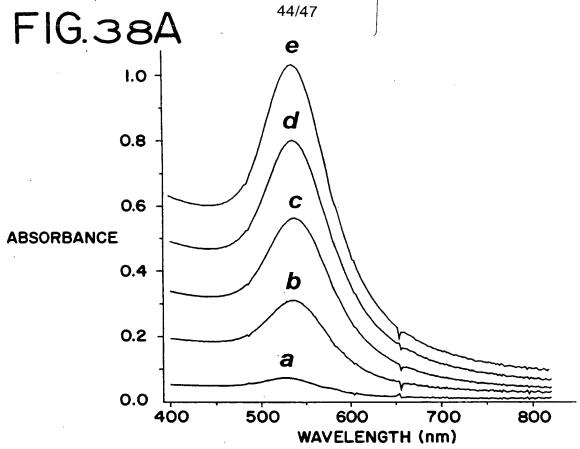


FIG.37B







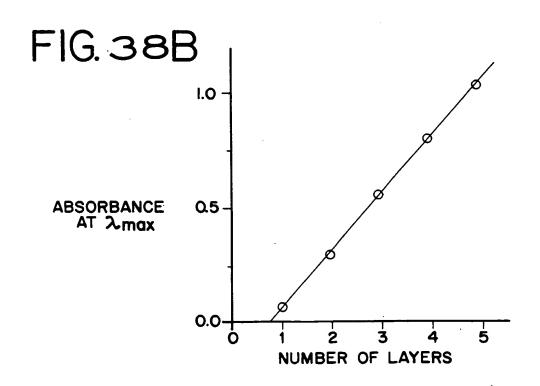




FIG. 39A

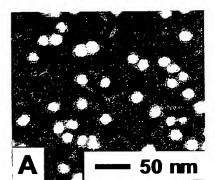
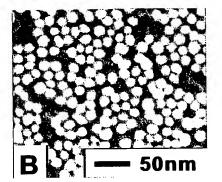
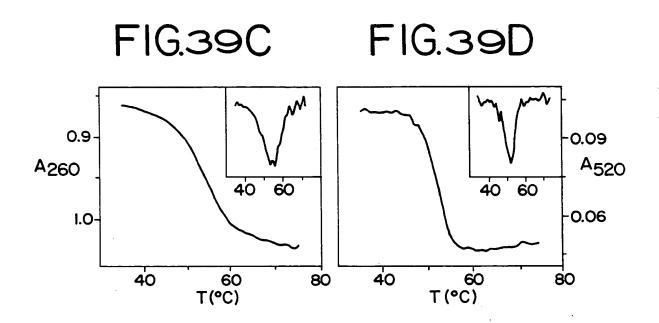
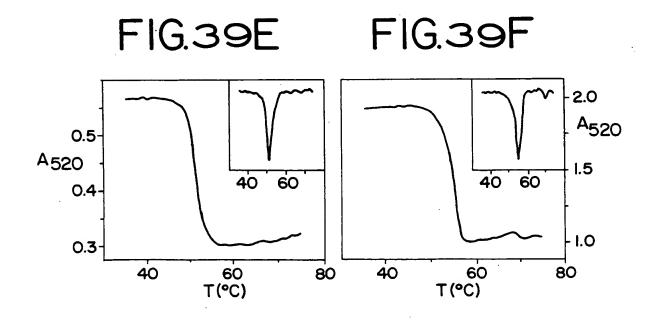


FIG. 39B











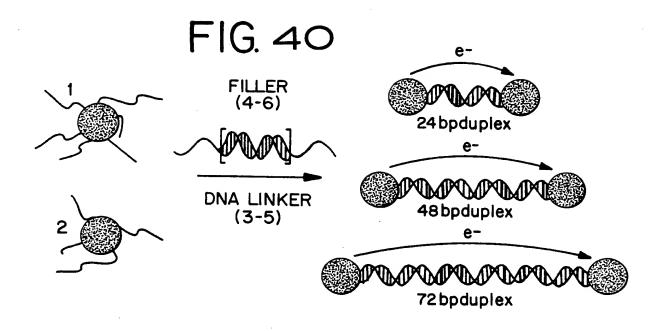


FIG. 41

